REMARKS

Claims 1 – 7 are pending in the application. Claims 1 – 7 have been amended. No new claims have been added. No new matter has been added by virtue of the amendments, support being found throughout the specification and from the pending claims.

The Examiner indicates that a substitute specification excluding the claims is required pursuant to 37 CFR 1.25(a). The Examiner indicates that the specification as filed contains two separate sections for experimental results. A substitute specification in accordance with 37 CFR 1.25(a) is being filed under separate cover.

The Examiner indicates that the listing of references in the specification is not a proper information disclosure statement. Applicants will file a proper information disclosure statement according to 37 CFR 1.98(b) under separate cover.

Claim Rejections- 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 1 – 7 under 35 USC 112, second paragraph, as being indefinite. Applicants respectfully traverse the rejection.

The Examiner argues that "claims 1 – 7 each recite neoplastic cell(s) which is/are 'representative' of cells constituting a tumor of interest (and) that the metes and bounds of the claims cannot be determined as the specification has not provided a definition of what constitutes a neoplastic cell representative of other tumor cells (Office Action p.4)."

Applicants direct the Examiner to paragraphs [0127] - [0129] of the published application. These passages describe both representative tumor cells constituting a lymphoma or leukemia, and the general essential requirements and characteristic features of the genetically modified cellular composition [see 0128]:

> [0127] A genetically altered neoplastic cell useful as an immunostimulatory agent against a lymphoma or leukemia of interest, said genetically altered neoplastic cell comprising: a cell of mammalian origin which is representative of the tumor cells constituting a lymphoma or a leukemia of interest; a genetically altered genome including at least one extra nucleotide segment comprising a viral vector and not less than one DNA sequence encoding molecule B7.1, intracellular adhesion molecule-1 (ICAM-1) and leukocyte function-associated antigen-3 (LFA-3) as specific products; the capacity to express molecule B7.1, intracellular adhesion molecule-1 (ICAM-1) and leukocyte

> function-associated antigen 3 (LFA-3) as discrete products and functional costimulatory molecules; and the capability to interact with and to activate CD4+ and CD8+ T-cell lymphocytes in-situ.
>
> [0128] Note the essential requirements and characteristic features of the genetically modified cellular composition: first, the tumor cell is of mammalian origin and must exemplify and represent a lymphoma or leukemia of choice. However, the actual source of origin for the mammalian tumor cell may be ex-vivo, in-vivo, or in-vitro. Second, the genetically altered genome of the mammalian tumor cell must be the consequence of an infection and transduction of the native genome by a TRICOM viral vector. Third, the genetically modified genome of the tumor cell has the capacity to express not less than three different exogenous genes or DNA sequences as discrete products and functional costimulatory molecules. These are the B7.1, ICAM-1, and LFA-3 molecules. Fourth, the genetic modifications to the native genome have created a new capacity for the tumor cell--the ability to interact with and to activate CD4+ and CD8+ lymphocytes in-situ.
>
> [0129] These genetically modified characteristics and features for the tumor cell constitute not only the essential requirements of the present invention, but also identify the novel and unforeseen attributes and capacities which are shared in common by all embodiments and formats constituting the subject matter as a whole which is the present invention. These requisite structural features and recited attributes are reflected and restated by the other aspects and alternative recitations for the genetically modified tumor cell.

Thus, Applicant's definition of "representative" cells is clearly supported in the specification. Accordingly, Applicants respectfully request withdrawal of the rejection and allowance of the claims.

The Examiner has further rejected claims 1 – 7 as being indefinite for reciting "at least one extra nucleotide segment comprising a viral vector and not less than one DNA sequence encoding B7.1, ICAM-1 and LFA-3 (Office Action p.4). The Examiner alleges that the limitation "not less than one DNA" is confusing. Applicants have amended the claims to read "at least one DNA sequence." Thus, Applicants respectfully request withdrawal of the rejection and allowance of the claims.

Claim Rejections- 35 U.S.C. § 102(b)

Claims 1 - 7 have been rejected under 35 U.S.C. § 102(b) as being anticipated by WO 00/34494 (Hodge et al; the '494 reference). Applicants respectfully traverse the rejection.

The instant invention teaches genetically altered neoplastic cells useful as immunostimulatory agents against a tumor of interest. The genetically altered neoplastic cells comprise a neoplastic cell of mammalian origin, a genetically altered genome including at least one extra nucleotide segment comprising a viral vector and at least one DNA sequence encoding molecule B7.1, intracellular adhesion molecule-1 (ICAM-1) and leukocyte function-associated antigen-3 (LFA-3) as specific products. The genetically altered neoplastic cells comprise the capacity to overexpress molecule B7.1, intracellular adhesion molecule-1 (ICAM-1) and leukocyte function-associated antigen-3 (LFA-3) as *discrete products and functional costimulatory molecules*, and the capability to interact with and to activate CD4+ and CD8+ T-cell lymphocytes in-situ (emphasis added).

In order to anticipate a claim, each and every element of the claim must be found in a single reference. This is discussed in the Manual of Patent Examining Procedure § 2131:

> "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the . . . claim." Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an ipsissimis verbis test, i.e., identity of terminology is not required. In re Bond, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

The '494 reference does not teach a recombinant viral vector that overexpresses molecule B7.1, intracellular adhesion molecule-1 (ICAM-1) and leukocyte function-associated antigen-3 (LFA-3) as *discrete products and functional costimulatory molecules*. At best, the '494 reference teaches a vector vaccine that expresses multiple costimulatory molecules to provide enhanced T-cell activation. Applicants direct the Examiner to the Abstract of the Invention, for example, which refers to "the synergistic effect of these costimulatory molecules." This is

different from the instant invention which teaches the genetically altered neoplastic cells have the capacity to overexpress B7.1, ICAM-1, and LFA-3 as discrete products that are functional costimulatory molecules. The mere fact that a cell can express costimulatory molecules on its surface does not necessarily alone determine or even indicate which costimulatory molecule is functional and that such a cell will efficaciously activate T cells. Different levels in the expression of costimulatory molecules affect and regulate the immunogenicity of a tumor; and such quantum differences in expression markedly influence the outcome and effectiveness of an antitumor response (see, for example, Viola, A. and A. Lanzavecchia, Science 273:104-106 (1996); filed with IDS).

Thus, Applicants respectfully request withdrawal of the rejection and allowance of the claims.

Claim Rejections- 35 U.S.C. § 102(e)

Claims 1 - 7 have been rejected under 35 U.S.C. § 102(e) as being anticipated by US Patent No. 6,969,609 (Schlom et al.; the '609 reference). Applicants respectfully submit that the invention as claimed is not anticipated by the '557 reference and respectfully traverse the rejection.

As stated above, the instant invention teaches genetically altered neoplastic cells useful as immunostimulatory agents against a tumor of interest. The genetically altered neoplastic cells comprise a neoplastic cell of mammalian origin, a genetically altered genome including at least one extra nucleotide segment comprising a viral vector and at least one DNA sequence encoding molecule B7.1, intracellular adhesion molecule-1 (ICAM-1) and leukocyte function-associated antigen-3 (LFA-3) as specific products. The genetically altered neoplastic cells comprise the capacity to overexpress molecule B7.1, intracellular adhesion molecule-1 (ICAM-1) and leukocyte function-associated antigen-3 (LFA-3) as discrete products and functional costimulatory molecules, and the capability to interact with and to activate CD4+ and CD8+ T-cell lymphocytes in-situ (emphasis added).

The Examiner argues that the '609 reference teaches a recombinant viral vector encoding all of the co-stimulatory molecules B7-1, ICAM-1 and LFA-3, and methods of using the vector to transducer tumor cells such that the transduced cells express all three of the encoded co-stimulatory proteins.

For the reasons stated above, the '609 reference does not teach a recombinant viral vector that overexpresses molecule B7.1, intracellular adhesion molecule-1 (ICAM-1) and leukocyte function-associated antigen-3 (LFA-3) as *discrete products and functional costimulatory molecules*. Thus, the '609 reference does not anticipate the instant claims.

Accordingly, Applicants respectfully request withdrawal of the rejection and allowance of the claims.

CONCLUSION

In view of the above amendment and remarks, Applicants believe the pending application is in condition for allowance.

Should the Examiner wish to discuss any of the amendments and/or remarks made herein, the undersigned attorney would appreciate the opportunity to do so.

Respectfully submitted,

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